Claims 13-19, added by the Preliminary Amendment filed February 13, 2001, find support in originally filed claims 1-12. Claims 13-19 and new claims 20-23 were only added to place original claims 1-12 in better conformity with U.S. Patent practice, but do not contain any additional subject matter that was not earlier claimed and examined in the parent PCT application. Therefore, no issue of new matter is raised and consequently the instant application fully complies with 37 C.F.R. § 1.496(b), which allows claim amendments as to form at any time during prosecution of the application. Accordingly, Applicants respectfully request that this objection be withdrawn.

III. Objections under 37 C.F.R. § 1.475

The Examiner objected to claims 9-12 and 16-19 as being directed to more than one utility. The Examiner argues that claims 9-12 and 16-19 should be rewritten or canceled so that one understandable method of use, in currently available form, is claimed in these claims. The Examiner suggested that Applicants pick one use from claims 12 and 19 and that these claims be written as "methods of treating" claims, picking one understandable utility in currently available form.

According to the Examiner, 37 C.F.R. § 1.475 provides for one method of use to be examined with the elected compounds. The Examiner argues that in addition to the compound, Applicants are entitled to have one clear, understandable utility examined with the compound. Applicants respectfully disagree.

All methods of use instantly claimed comply with the unity of invention standard of rule 1.475. The International Searching Authority (ISA) has already examined the

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present application during the PCT stage and found that unity of invention exists for the instantly claimed subject matter. Proof of this statement is found in the following facts: a) original claims 1-12 were examined together (See Preliminary Examination Report of the corresponding PCT application), b) the ISA did not issue an "Invitation to Restrict or Pay Additional Fees", which is the normal practice when lack of unity is found, and c) a lack of unity finding is not mentioned in the Preliminary Examination Report, which is the alternative option when Applicants are not invited to restrict or pay additional fees (See PCT Rule 68.1). Original claim 12 of the present application contains all uses instantly claimed and, together with claims 1-11, was found to be part of only one invention by the ISA. Therefore, Applicants are entitled to have the methods of use in present claims 12 and 19, which are encompassed by original claim 12, examined in this application. Moreover, unity of invention exists because all uses of the compounds of the invention are related directly or indirectly to their disclosed property of guanylate cyclase activation, which corresponds to the unifying technical feature required by rule 1.475.

IV. Rejections under 35 U.S.C. §§ 101 and 112

The Examiner rejected claims 9, 11, 12, 16, 18, and 19 as violating 35 U.S.C. § 101 and 35 U.S.C. § 112 because, according to the Examiner, these claims are drafted as "use" claims. In light of the cancellation of claims 9 and 16 and the amendments to claims 10-12 and 17-19, the Examiner's arguments are now moot and Applicants respectfully request that these rejections be withdrawn. Applicants note that the scope of the amended claims has not changed due to these modifications in format.

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The Examiner also argued that claims 11 and 18 should be cancelled, alleging that activation of soluble guanylate cyclase does not qualify as a real-world utility. In the Examiner's view, screen tests or laboratory tests are not accepted as real-world utilities. The Examiner cites the 1995 PTO Guidelines on Utility Requirements (the Guidelines, BNA's Patent and Trademark Journal, vol. 50, p. 295-309, July 20, 1995) as support for the above statement (the Guidelines at p. 298, col. 2). Applicants respectfully disagree.

Contrary to the Examiner's assertion, the cited section of the Guidelines does not indicate that screening assays have no utility, rather, this section merely states that the fact that a screening assay is useful in a research setting does not address whether the invention is useful. In other words, the fact that a screening assay is useful in a research setting may not be helpful in determining utility for that assay, but this fact does not necessarily negate utility of the screening assay.

Furthermore, the Guidelines clearly state "a disclosure that identifies a particular biological activity of a compound and explains how that activity can be utilized in a particular therapeutic application of the compound does contain an assertion of specific utility." Id. at p. 302, paragraph bridging col. 1-2. One embodiment of Applicants' invention indicates that the compounds of the invention "bring about strong guanylate cyclase activation, on account of which they are suitable for the therapy and prophylaxis of illnesses associated with a low cGMP level." Specification at p. 3, line 36 to p. 4, line 2. The specification at page 2, lines 26-35 provides examples of such illnesses. Accordingly, claims 11 and 18 have utility and Applicants respectfully request that this rejection be withdrawn.

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The Examiner also rejected claim 9 for not meeting the utility guidelines stated in *Brenner v. Manson* 148 U.S.P.Q. 689. Since Applicants have cancelled claim 9, the Examiner's rejection is now moot. Accordingly, Applicants respectfully request that this rejection be withdrawn.

V. Rejections under 35 U.S.C. § 112

The Examiner rejected claim 15 under 35 U.S.C. § 112, second paragraph. According to the Examiner, claim 15 does not indicate what "activating" means. Applicants respectfully traverse this rejection.

Applicants respectfully remind the Examiner that the claims should be analyzed in light of the specification. Page 14, lines 26-33 of the specification indicates that activation can include the conversion of the hydroxypyrimidine of formula IV into a reactive derivative thereof capable of reacting with an amine of formula VI. An example of such activation is the conversion of a hydroxypyrimidine of formula IV into a 4-halopyrimidine by reaction with a phosphorous halide. Therefore, the specification conveys to the skilled artisan the meaning of "activating" and consequently claims 8 and 15 are not indefinite with respect to "activating." Accordingly, Applicants respectfully request that this rejection be withdrawn.

The Examiner rejected claims 1-7, 13, and 14 under 35 U.S.C. § 112, first and second paragraphs. According to the Examiner, mixtures in all ratios made by any means are not supportable. The Examiner further indicates that man-made mixtures

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are not in class 544, with the pyrimidine, but in class 252 and requests clarification. Applicants respectfully traverse this rejection.

The phrase mixtures "in all ratios" of the compounds of the invention is self-describing and the skilled artisan would fully understand the metes and bounds of this term. These mixtures in all ratios refer to mixtures of the compounds of the invention in all ratios, including mixtures of stereoisomers. *See e.g.*, specification at p. 10 line 34 to p. 11 line 17. Applicants have amended claim 1 in this regard in order to more clearly define the subject matter of the invention. The preparation of mixtures "in all ratios" of the compounds of the invention can be easily accomplished by the skilled artisan with no more knowledge than what is already known in the art. For example, some methods for the preparation of compounds of the invention produce mixtures of stereoisomers, from which the individual compounds can be isolated by known methods in the art such as chromatography or crystallization. Specification at p. 11, lines 8-10. Additionally, individual stereoisomers may be prepared by the use of sterochemically homogeneous starting materials or via stereoselective synthesis. Specification at p. 11, lines 10-12. In general, mixtures in all ratios may be prepared, for example, by simply adding one component to another until the desired ratio is reached. The process may be repeated for any component in the mixture. Therefore, claims 1-7, 13, and 14 are not indefinite with respect to mixtures "in all ratios" and Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph be withdrawn.

Moreover, by including the term "in all ratios" in the language of the claims, Applicants are merely defining what would be implicitly understood if this term was

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absent and the claims were to recite simply "mixtures [of the compounds of the invention]". That is, a claim drawn to a mixture when the ratio of the components of the mixture is not specified clearly encompasses a mixture of the components present at any ratio. In view of the foregoing arguments, claims 1-7, 13, and 14 have full 35 U.S.C. § 112 support and Applicants respectfully request that this rejection be withdrawn.

VI. Rejections under 35 U.S.C. § 103

The Examiner rejected claim 1 under 35 U.S.C § 103, as being unpatentable over Chokai *et al.*, European Patent Application No. EP 555,478. The Examiner indicates that A in *Chokai* is phenyl, as is R^3 in formula (I) of the compounds of the present invention, and that B in *Chokai* is methyl, while the corresponding group in the instant invention, R^4, is ethyl. The Examiner also indicates that R^4 here and B in *Chokai* may be trifluoromethyl or phenyl and that R^3 in *Chokai* corresponds to R^1R^2N in the present application. Applicants respectfully traverse this rejection.

Chokai does not disclose any of the compounds of the invention and does not teach nor suggest the use of the compounds disclosed therein as activators of guanylate cyclase. Furthermore, the Examiner has failed to provide any motivation the skilled artisan would have to modify the compounds of *Chokai* to prepare compounds claimed in the present invention. The Examiner is respectfully reminded that "obvious to try" modifications do not necessarily constitute a valid basis for an obviousness rejection. *In re Tomlinson*, 363 F.2d 928, 150 U.S.P.Q. 623. Accordingly, absent the

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requisite motivation, it would not have been obvious to modify one of the groups in the compounds in *Chokai* to arrive at the compounds of the present invention.

However, with the sole purpose of expediting prosecution, Applicants have broadened the proviso of claim 1. Applicants reserve the right to pursue protection for the presently disclaimed subject matter in a divisional application.

The compounds of the present claim 1 are sufficiently different from the compounds disclosed in *Chokai* to be considered patentable over the prior art. Indeed, with respect to the Examiner's assertion that "R^4 here is also trifluoromethyl and phenyl, as is B in [*Chokai*]", Applicants note that according to the proviso in claim 1, R^4 cannot be trifluoromethyl under the conditions when B is trifluoromethyl in *Chokai*. That is, claim 1 does not encompass any of the compounds disclosed in *Chokai* when B is trifluoromethyl. Furthermore, when the group B in *Chokai* is phenyl, the group A in the 2-position of the pyrimidine ring is methyl, trifluoromethyl, or tert-butyl, but cannot be phenyl. *Chokai* at page 3 line 35. In contrast, in the compounds of the invention, the group R^3 in the 2-position of the pyrimidine ring (equivalent to A in *Chokai*) is always phenyl (substituted or unsubstituted).

Therefore, not only do the compounds of the invention differ from the compounds of *Chokai* when B is either trifluoromethyl or phenyl, but, for the reasons discussed, nothing in *Chokai* would have motivated the skilled person to modify *Chokai*'s compounds to produce the presently claimed compounds. Accordingly, Applicants respectfully request that this rejection be withdrawn.

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The Examiner also rejected claims 8 and 15 as being dependent on a rejected claim. In light to the foregoing remarks and amendments, claims 1 and 5, from which claims 8 and 15 depend, are in condition for allowance and Applicants respectfully request that this rejection be withdrawn.

VII. Information Disclosure Statement

The Examiner returned the PTO 1449 forms Applicants filed on February 13, 2001. However, the Examiner did not initial several abstracts listed on pages 4 and 5 of the 1449 form, apparently because no date was listed on the 1449 form. However, the publication date is listed on the face of each abstract and on each patent application. Applicants respectfully request that the Examiner initial and return the aforementioned PTO 1449 form to Applicants.

Conclusions

In view of the foregoing amendments and remarks, Applicants respectfully request the examination of this application and the timely allowance of the pending claims.

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If there is any fee due in connection with the filing of this Preliminary Amendment, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

By: Carlos M Tellez

Carlos M. Tellez
Reg. No. 48,638

Dated: January 16, 2002

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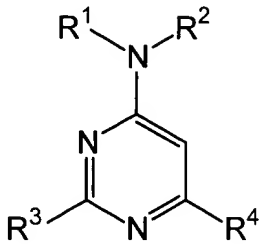
Appendix to Response and Amendment dated January 16, 2002

1. A compound of the formula I,



I

in which

R^1 is $(C_1\text{-}C_8)$-alkyl, which can be substituted by one or more identical or different substituents chosen from ~~the group consisting of~~ hydroxyl, $(C_1\text{-}C_4)$-alkoxy, $(C_1\text{-}C_4)$-alkyl-$S(O)_m$-, R^5R^6N and aryl; $(C_3\text{-}C_9)$-cycloalkyl, which can be substituted by one or more identical or different substituents chosen from ~~the group consisting of~~$(C_1\text{-}C_4)$-alkyl, hydroxyl and amino; or ~~the~~ a radical of a 5-membered to 7-membered saturated heterocyclic ring ~~which~~ that contains one or two identical or different hetero ring members chosen from ~~the group consisting of~~O, NR^7 and $S(O)_m$ and ~~which~~ that can be substituted by one or more identical or different substituents chosen from ~~the group consisting Of~~ $(C_1\text{-}C_4)$-alkyl and aryl-$(C_1\text{-}C_4)$-alkyl-;

and

R^2 is hydrogen, $(C_1\text{-}C_8)$-alkyl, which can be substituted by one or more identical or different substituents chosen from ~~the group consisting of~~ hydroxyl, $(C_1\text{-}C_4)$-alkoxy, $(C_1\text{-}C_4)$-alkyl-$S(O)_m$-, R^5R^6N and aryl; $(C_3\text{-}C_9)$-cycloalkyl, which can be substituted by one or more identical or different substituents

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chosen from ~~the group consisting of~~ (C_1-C_4)-alkyl, hydroxyl and amino~~,~~; or the radical of a 5-membered to 7-membered saturated heterocyclic ring ~~which~~ that contains one or two identical or different hetero ring members chosen from ~~the group consisting of~~ O, NR^7 and $S(O)_m$ and that ~~which~~ can be substituted by one or more identical or different substituents~~;~~ chosen from ~~the group consisting of~~ (C_1-C_4)-alkyl and aryl-(C_1-C_4)-alkyl-; or

R^1R^2N is a radical, bonded via a ring nitrogen atom, of a 5-membered to 7-membered saturated heterocyclic ring ~~which~~that, in addition to the nitrogen atom carrying the radicals R^1 and R^2, can contain a further hetero ring member chosen from ~~the group consisting of~~ O, NR^7 and $S(O)_m$ and that ~~which~~ can be substituted by one or more identical or different substituents chosen from ~~the group consisting of~~ (C_1-C_4)-alkyl, hydroxyl, (C_1-C_4)-alkoxy, R^8R^9N, hydroxycarbonyl, (C_1-C_4)-alkoxycarbonyl and R^8R^9N-CO-;

R^3 is phenyl, which can be substituted by one or more identical or different substituents chosen from ~~the group consisting of~~ halogen, (C_1-C_4)-alkyl, phenyl, CF_3, NO_2, OH, -O-(C_1-C_4)-alkyl, -O-(C_2-C_4)-alkyl-O-(C_1-C_4)-alkyl, (C_1-C_2)-alkylenedioxy, NH_2, -NH-(C_1-C_4)-alkyl, N((C_1-C_4)-alkyl)$_2$, -NH-CHO, -NH-CO-(C_1-C_4)-alkyl, -CN, -CO-NH_2, -CO-NH-(C_1-C_4)-alkyl, -CO-N((C_1-C_4)-alkyl)-$_2$, -CO-OH, -CO-O-(C_1-C_4)-alkyl, -CHO and –CO-(C_1-C_4)-alkyl;

R^4 is (C_2-C_5)-alkyl, trifluoromethyl or phenyl, which can be substituted by one or more identical or different substituents chosen from ~~the group consisting of~~ halogen, (C_1-C_4)-alkyl, phenyl, CF_3, NO_2, OH, -O-(C_1-C_4)-alkyl, -O-(C_2-C_4)-alkyl-O-(C_1-C_4)-alkyl, (C_1-C_2)-alkylenedioxy, NH_2, -NH-(C_1-C_4)-alkyl, N((C_1-C_4)-alkyl$_2$, -NH-CHO, -NH-CO-(C_1-C_4)-alkyl, -CN, -CO-NH_2, -CO-

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NH-(C_1-C_4)-alkyl, -CO-N((C_1-C_4)-alkyl$_2$, -CO-OH, -CO-O-(C_1-C_4)- alkyl, -CHO and –CO-(C_1-C_4)-alkyl;

R^5 and R^6 are identical or different radicals chosen from ~~the group consisting of~~ hydrogen and (C_1-C_4)-alkyl; or the group R^5R^6N is a radical, bonded via a ring nitrogen atom, of a 5-membered to 7-membered saturated or saturated heterocyclic ring thatwhich, in addition to the nitrogen atom carrying the radicals R^5 and R^6, can additionally contain as a further hetero ring member an oxygen atom, a group $S(O)_m$ or a nitrogen atom and that ~~which~~ can carry on ring carbon atoms one or more identical or different substituents chosen from ~~the group consisting of~~ (C_1-C_4)-alkyl, hydroxyl and amino and that can carry on a ring nitrogen atom a radical R^7;

R^7 is hydrogen, (C_1-C_4)-alkyl, aryl-(C_1-C_4)-alkyl-, hydroxy-(C_1-C_4)-alkyl, hydroxycarbonyl-(C_1-C_4)-alkyl-, ((C_1-C_4)-alkoxycarbonyl)-(C_1-C_4)-alkyl, R^8R^9N-CO-(C_1-C_4)-alkyl-, R^{10}-SO_2- or aryl~~,~~; where R^7, if this group is present on a piperazino radical representing R^1R^2N, cannot be carbocyclic aryl or carbocyclic aryl-(C^1-C^4)-alkyl;

R^8 and R^9 are identical or different radicals chosen from ~~the group consisting of~~ hydrogen and (C_1-C_4)-alkyl;

R^{10} is (C_1-C_4)-alkyl, aryl or R^8R^9N;

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aryl is phenyl, naphthyl or heteroaryl, ~~which can~~ all of which can be substituted by one or more identical or different substituents chosen from ~~the group consisting of~~ halogen, (C_1-C_4)-alkyl, phenyl, CF_3, NO2, OH, -O-(C_1-C_4)-alkyl, O-(C_2-C_4)-alkyl-O-(C_1-C_4)-alkyl, (C_1-C_2)-alkylenedioxy, NH_2, -NH-(C_1-C_4)-alkyl, -N$((C_1-C_4)$-alkyl$_2$, -NH-CHO, -NH-CO-(C_1-C_4)-alkyl, -CN, CO-NH_2, -CO-NH-(C_1-C_4)-alkyl, -CO-N$((C_1-C_4)$-alkyl$_2$, -CO-OH, -CO-O-(C_1-C_4)-alkyl, -CHO and –CO-(C_1-C_4)-alkyl;

heteroaryl is the radical of a monocyclic 5-membered or 6-membered aromatic heterocycle or of a bicyclic 8-membered to 10-membered aromatic heterocycle, each of which contains one or more identical or different ring heteroatoms chosen from ~~the group consisting of~~ N, O and S;

m is 0, 1 or 2;

~~in all their stereoisomeric forms and mixtures thereof in all ratios, and their physiologically tolerable salts,~~

or a stereoisomeric form of a compound of formula I,

or a mixture of stereoisomeric forms of compounds of formula I in all ratios,

or a physiologically tolerable salt of a compound of formula I,

or a physiologically tolerable salt of a stereoisomeric form of a compound of formula I;

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compounds of the formula I being excluded in which, simultaneously, R^4 is ethyl, tert-butyl, or trifluoromethyl; R^3 is phenyl, which can be substituted by one or two identical or different substituents chosen from ~~the group consisting of~~ halogen, OH, -O-R^{11} and CF_3, R^1R^2N is R^{11} -NH-, $(R^{11})_2N$- or $R^{12}R^{13}N$-$(CH_2)_p$-NH-; p is 2 or 3; R^{11} is saturated unsubstituted $(C_1$-$C_4)$-alkyl; and R^{12} and R^{13} are identical or different radicals chosen from ~~the group consisting of~~ hydrogen and R^{11} or the group $R^{12}R^{13}N$ is a radical, bonded via a ring nitrogen atom, of a 5-membered or 6-membered saturated heterocyclic ring ~~which~~that, in addition to the nitrogen atom carrying the radicals R^{12} and R^{13}, can additionally contain as a further hetero ring member an oxygen atom, a sulfur atom or a nitrogen atom and ~~which~~ that can be substituted by an aryl substituted by one or two identical or different substituents chosen from ~~the group consisting of~~ halogen, OH, -O-R^{11}, and CF_3.

2. A compound of ~~the formula I as claimed in~~ claim 1, in which

R1 is $(C_1$-$C_8)$-alkyl, which can be substituted by one or more identical or different substituents, chosen from ~~the group consisting of~~ hydroxyl, (C1-C4)-alkoxy, (C1-C4)-alkyl-$S(O)_m$-, R^5R^6N and aryl; or is $(C_3$-$C_9)$-cycloalkyl, which can be substituted by one or more identical or different substituents chosen from ~~the group consisting of~~ $(C_1$-$C_4)$-alkyl, hydroxyl and amino; and

R^2 is hydrogen, $(C_1$-$C_8)$-alkyl, which can be substituted by one or more identical or different substituents chosen from ~~the group consisting of~~ hydroxyl, $(C_1$-$C_4)$-alkoxy, $(C_1$-$C_4)$-alkyl-$S(O)_m$-, R^5R^6N and aryl; or is $(C_3$-$C_9)$-cycloalkyl, which can be substituted by one or more identical or different substituents chosen from ~~the group consisting of~~ $(C_1$-$C_4)$-alkyl, hydroxyl and amino; or

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R^1R^2N is a radical, bonded via a ring nitrogen atom~~,~~ of a 5-membered, 6-membered or 7-membered saturated heterocyclic ring thatwhich~~which~~, in addition to the nitrogen atom carrying the radicals R^1 and R^2, can additionally contain as a further hetero ring member an oxygen atom, a group $S(O)_m$ or a nitrogen atom carrying a radical R^7 and that ~~which~~ can be substituted by one or more identical or different substituents chosen from ~~the group consisting of~~ $(C_1$-$C_4)$-alkyl, hydroxyl, $(C_1$-$C_4)$-alkoxy, R^8R^9N, hydroxycarbonyl, $(C_1$-$C_4)$-alkoxycarbonyl and R^8R^9N-CO~~,~~ ~~; in all its stereoisomeric forms and mixtures thereof in all ratios, or its physiologically tolerable salts.~~

3. A compound of ~~the formula 1 as claimed in~~ claim 1, in which R^1 is $(C_1$-$C_4)$-alkyl, which can be substituted by one or more identical or different substituents chosen from ~~the group consisting of~~ hydroxyl, $(C_1$-$C_4)$-alkoxy, $(C_1$-$C_4)$-alkyl-$S(O)_m$-, R^5R^6N and aryl, or $(C_3$-$C_9)$-cycloalkyl, which can be substituted by one or more identical or different substituents chosen from ~~the group consisting of~~ $(C_1$-$C_4)$-alkyl, hydroxyl and amino, and R^2 is hydrogen~~,~~ ~~;~~ or R^1 and R^2 are identical or different $(C_1$-$C_4)$-alkyl, which can be substituted by one or more identical or different substituents chosen from ~~the group consisting of~~ hydroxyl, $(C_1$-$C_4)$-alkoxy, $(C_1$-$C_4)$-alkyl-$S(O)_m$-, R^5R^6N and aryl~~;~~

~~in all its stereoisomeric forms and mixtures thereof in all ratios, or its physiologically tolerable salts~~.

4. A compound of ~~the formula I as claimed in~~ claim 1, in which R^1 is $(C_3$-$C_9)$-cycloalkyl, which can be substituted by one or more identical or different substituents chosen from ~~the group consisting of~~ $(C_1$-$C_4)$-alkyl, hydroxyl and amino, and R^2 is hydrogen~~; in all its stereoisomeric forms and mixtures thereof in all ratios, or its physiologically tolerable salts~~.

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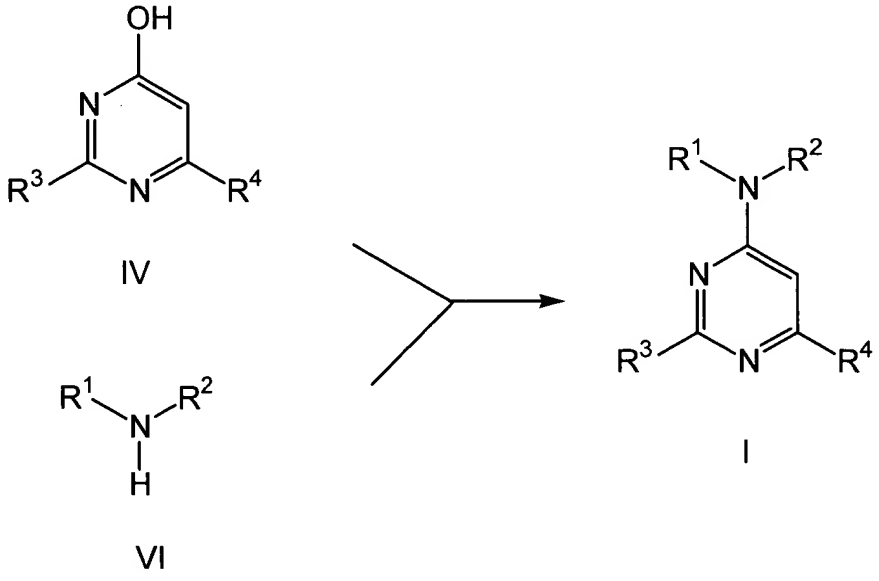
5. A compound of ~~the formula I as claimed in~~ claim 1, in which R^1R^2N- is an unsubstituted or substituted radical chosen from ~~the group consisting of~~ piperidino, morpholino and thiomorpholino (and its S-oxide and S,S-dioxide) and piperazino~~; in all its stereoisomeric forms and mixtures thereof all ratios, or its physiologically tolerable salts~~.

6. A compound of ~~the formula I as claimed in~~ claim 1, in which R^3 is substituted phenyl~~; in all its stereoisomeric forms and mixtures thereof in all ratios, or its physiologically tolerable salts~~.

7. A compound of the formula I as claimed in claim 1, in which R^4 is $(C_3$-$C_4)$-alkyl~~; in all its stereoisomeric forms and mixtures thereof in all ratios, or its physiologically tolerable salts~~.

8. A process for the preparation of at least one compounds ~~of the formula I as claimed in~~ claim 1, which comprises activating a 4-hydroxypyrimidine of the formula IV and then reacting it with an amine of a formula VI to produce a compound of formula I,



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and optionally reacting a compound of formula I with a suitable reagent to form a pharmaceutically acceptable salt.~~where R^1, R^2, R^3 and R^4 have the meanings indicated in claim 1~~

10. A ~~pharmaceutical preparation~~ composition, which contains one or more compounds of ~~the formula I as claimed in~~ claim 1 ~~and/or its/their physiologically tolerable salts~~, and a ~~pharmaceutically tolerable~~ carrier.

11. A method for activating soluble guanylate cyclase, comprising administering to a patient in need thereof at least one compound of ~~the formula I as claimed in~~ claim 1, ~~and/or its physiologically tolerable salts for use as activators of soluble guanylate cyclase.~~

12. A method of treating a medical condition, comprising administering to a patient in need thereof an effective amount of at least one compound of ~~the formula I as claimed in~~ claim 1 ~~and/or its physiologically tolerable salts for use in the therapy or prophylaxis of~~, wherein the medical condition is chosen from at least one of cardiovascular disorders, endothelial dysfunction, diastolic dysfunction, atherosclerosis, high blood pressure, angina pectoris, thromboses, restenoses, myocardial infarct, strokes, cardiac insufficiency, pulmonary hypertension, erectile dysfunction, bronchial asthma, chronic renal insufficiency, diabetes, ~~or~~ liver cirrhosis, ~~or for~~ and improving restricted learning capacity or memory power.

13. A compound of ~~the formula I as claimed in~~ claim 5, in which R^3 is substituted phenyl~~; in all its stereoisomeric forms and mixtures thereof in all ratios, or its physiologically tolerable salts.~~

14. A compound of ~~the formula I as claimed in~~ claim 5, in which R^4 is $(C_3$-$C_4)$-alkyl~~; in all its stereoisomeric forms and mixtures thereof in all ratios, or its physiologically tolerable salts~~.

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15. A process for the preparation of at least one compounds of ~~the formula I as claimed in~~ claim 5, which comprises activating a 4-hydroxypyrimidine of the formula IV and then reacting it with an amine of a formula VI,

~~where R^1, R^2, R^3 and R^4 have the meanings indicated in claim 1.~~

17. A ~~pharmaceutical preparation~~ composition, which contains one or more compounds of ~~the formula I as claimed in~~ claim 5 ~~and/or its/their physiologically tolerable salts~~ and a ~~pharmaceutically tolerable~~ carrier.

18. A method for activating soluble guanylate cyclase, comprising administering to a patient in need thereof at least one compound of ~~the formula I as claimed in~~ claim 5, ~~and/or its physiologically tolerable salts for use as activators of soluble guanylate cyclase.~~

19. A method of treating a medical condition, comprising administering to a patient in need thereof an effective amount of at least one compound of ~~the formula I as claimed in~~ claim 5 ~~and/or its physiologically tolerable salts~~, wherein the medical condition is chosen from ~~for use in the therapy or prophylaxis of~~ cardiovascular disorders, endothelial dysfunction, diastolic dysfunction, atherosclerosis, high blood pressure, angina pectoris, thromboses, restenoses, myocardial infarct, strokes, cardiac insufficiency, pulmonary hypertension, erectile dysfunction, bronchial asthma, chronic renal insufficiency, diabetes, ~~or~~ liver cirrhosis, ~~or for~~ and improving restricted learning capacity or memory power.

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